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Attorney Docket # 4493-19C/RCE

Patent

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of

Shalom Z. Hirschman

Serial No.: 09/316,624

Filed: May 21, 1999

For: A Method For Treating Autoimmune Diseases

Examiner:

Group Art:

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Board of Patent Appeals and Interferences
Washington, D.C. 20231

APPEAL BRIEF

This is an appeal, pursuant to 37 C.F.R. §1.192(a) from the decision of the Examiner in the above-identified application, as set forth in the Final Office Action wherein the Examiner finally rejected appellant's claims. The rejected claims are reproduced in the Appendix A attached hereto. A Notice of Appeal was filed on May 17, 2002. This Appeal Brief is being submitted in triplicate.

The fee of $160.00 for filing an Appeal Brief (Small Entity) pursuant to 37 C.F.R. §1.17(f) is submitted herewith.

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BOARD OF PATENT APPEALS AND INTERFERENCES

Statement of Real Party in Interest

Advanced Viral Research Corporation, the owner of an undivided entire interest of the present application, is the real party in interest.

Statement of Related Appeals and Interference

There is no appeals and interference relating to the present application.

Status of Claims

Claims 1-4 are rejected.

Status of Amendment

No amendment has been made after the Final Action.

Summary of Invention

The present invention is directed to a method of ameliorating rheumatoid arthritis by injecting a patient with an effective amount of a pharmaceutical product, namely, Product R, which is a generic name given by applicants to their proprietary product. The effective amount of Product R was determined to be in a range from about 2.5 microliters to about 40 microliters per kilogram of body weight per day. More detailed description of the present invention can be found from page 12, line 9 to page 13, line 15; and from page 14, line 20 to page 15, line 12.

Issues

1. Whether claims 1-4 are anticipated by U.S. Pat. No. 5,849,196 to Kochel under 35 U.S.C. 102(e).

2. Whether the claim language "an effective symptom ameliorating amount in a range from about 2.5 microliters to about 40 microliters per kilogram of body weight per day" recited in claim 1 is indefinite under 35 U.S.C. 112, second paragraph.

ARGUMENT

None of the claims is anticipated by U.S. Pat. No. 5,849,196 (the '196 patent) under 35 U.S.C. 102(e) because the '196 patent fails to teach each and every element recited in each individual claim.

The rejection to claims 1-4 under 35 U.S.C. 112, second paragraph, is erroneous due to the Examiner's mischaracterization of the nature of the drug recited in the claims for treating rheumatoid arthritis by ignoring the teachings in the present application.

I. Factual Background

Rheumatoid arthritis is a systemic, chronic, inflammatory autoimmune disease that affects principally the joints and sometimes many other organs and tissues throughout the body. The disease is characterized by a nonsupporative proliferative synovitis, which in time leads to the destruction of articular cartilage and progressive disabling arthritis. The disease is caused by persistent and self-perpetuating inflammation resulting from immunologic processes taking place in the joints. As is the case with most autoimmune diseases, the trigger that initiates the immune reaction remains unidentified. Both humoral and cell mediated immune responses are involved in the pathogenesis of rheumatoid arthritis. The majority of patients have elevated levels of serum immunoglobulins and essentially all patients have an antibody called rheumatoid factor (RF) directed against a component of another antibody class.

The invention at issue is directed to a method for treating rheumatoid arthritis using a drug named as "Product R", a composition containing peptides and nucleic acids. Product R is designed to be administered to the patients by injection according to specified dosage regimens. Claim 1 is representative, which reads:

> "A method of ameliorating a symptom of rheumatoid arthritis in a patient suffering from rheumatoid arthritis, comprising parenterally administering to said patient an effective symptom ameliorating amount of Product R in a range from about 2.5 microliters to about 40 microliters per kilogram of body weight per day in a pharmaceutically acceptable formulation."

It is undisputed that the claim is fully supported by the specification. Since "Product R" is a complex pharmaceutical composition containing multiple peptides and nucleic acids, the

specification explicitly sets forth the manufacturing processes so as to enable a person of ordinary skill in the art to make this product. See Spec. pp 10-12. Also indicated in the specification is that "Product R" is preferably administered to the patients in its original liquid form without being further formulated. See Spec. p. 13, ln. 3.

The Examiner rejects claims 1-4, under 35 U.S.C. 102(e), as being anticipated by U.S. Pat. No. 5,849,196 to Kochel (hereinafter "Kochel" or "the '196 patent").

The '196 patent is directed to an improvement of a conventional pharmaceutical composition also containing peptides and nucleic acids and the method of making such composition. The composition resulting from the improvement ("improved composition") described in the '196 patent is entirely different from "Product R", as evidently shown by its manufacturing process and physical, chemical and biological properties.

First, the improve composition in the '196 patent is prepared based on the "conventional composition". As shown below, the conventional composition and Product R do not share the same quantities of the raw components to begin with:

Starting Materials (in 10 L)	**The '196 patent**	**Product R**
Casein	250 grams	140 grams
Beef peptone	150 grams	68.4 grams
Serum albumin	15 grams	13 grams
RNA	80 grams	88 grams
NaOH	75 grams	66 grams

See Spec. p. 10, ln. 5; The '196 Patent, col. 5, ln. 11. It is inconceivable that different initial materials would result in the same composition.

In addition, the process for the conventional composition in the '196 patent requires a intermediate solution after first autoclaving to be cooled at a temperature "somewhat below room temperature", see The '196 Patent, col. 5, ln. 27, whereas the process for Product R requires the

autoclaved solution to stay at 3-8 °C for at least six hours, see Spec. p. 10, ln. 12. Known to a person of ordinary skill in the art, different cooling processes result in different amounts of precipitation.

Furthermore, the process for the conventional composition in the '196 patent requires several pH adjustments during its manufacturing process, see The '196 Patent, col. 5, ln. 31-45, whereas Product R requires only one pH adjustment at the end of the process, see Spec. p.10, ln. 18. It is also commonly known that a precipitation usually occurs whenever the pH of the solution is adjusted.

As a result, the above process in the '196 patent yields a composition, i.e., the "conventional composition", having a molecular weight range of 1-25 kDa, The '196 Patent, col. 2, ln. 5, a UV absorption profile shown in Figure 5, id., Figure 5, and inhibitory effect on phagocytosis, id., col. 9, ln. 15; whereas Product R is a product having molecular weight range up to 14 kDa, a UV absorption profile shown in Figure 1 of U.S. Pat. No. 6,303,153[1], and no inhibitory effect on phagocytosis, as shown in the following table:

	MW	**UV Absorbance**		**Inhibition of Phagocytosis**
		$A_{260/280}$	$A_{260/230}$	
Reticulose®	1-25 kDa*	2.839*	1.198*	No*
Product R	< 14 kDa#	1.998#	1.359#	Yes#

* *See* U.S. Pat. No. 5,849,196
# *See* U.S. Pat. No. 6,303,153

It suffices to say that the "conventional composition" described in the '196 patent is not Product R.

[1] The chemical, physical and biological properties of Product R have been analyzed and are fully described in U.S. Pat. No. 6,303,153.

According to the '196 patent, this conventional composition is further divided into two portions, a high molecular weight portion (MW > 8-15 kDa) and a low molecular weight portion. (MW < 8-15 kDa) to produce the improved composition, which is the claimed subject matter of the '196 patent.

In connection with the invention, the '196 patent asserts certain utilities of the invention including a potential use for treating autoimmune diseases, which is described in the following paragraph:

> "Further, although the lower weight active components (MW <8-15 kDa) of the composition are not effective s antiviral agents, they are effective in treating auto immune diseases such as non-Hodgkins Lymphoma, Adult Onset Leukemia, AIDS, Lupus, Scleroderma, Epstein Barr virus, Cytomegalovirus, Chronic Fatigue Syndrome, Candidiasis, Rheumatoid and Osteo Arthritis, etc. Thus, the active components of the conventional composition may be segregated according to molecular weight and the different resulting groups of components may be selectively used to treat different viruses and auto immune diseases accordingly."

See The '196 Patent, col. 3, ln. 1-11.

This comment becomes the sole basis underlying the Examiner's rejection to claims 1-4 at issue under 35 U.S.C. 102(e).

II. The '196 Patent Fails to Teach Each and Every Element Recited in the Claims.

Anticipation under 35 U.S.C. Section 102(e) requires that "each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros., Inc. v. Union Oil Co.* , 814 F.2d 628, 631, 2 U.S.P.Q.2d 1051, 1053 (Fed. Cir. 1987). Also *see Lewmar Marine, Inc. v. Barient, Inc.*, 827 *F.2d 744, 747, 3*

USPQ2d 1766, 1767 (Fed. Cir. 1987); Advanced Micro-Devices, Inc., 848 F.2d 1560, 1570 [7 USPQ2d 1057] (Fed. Cir.), cert. denied, 488 U.S. 892 (1988).

A comparison between claim 1 of the present invention and the teaching of the '196 patent clearly shows that the '196 patent does not contain each and every element set forth in claim 1.

1. The '196 patent fails to teach the use of Product R for treating rheumatoid arthritis

Claim 1 requires that Product R is administered to the rheumatoid arthritis patients, while the '196 patent merely suggests using the "low molecular weight portion" of the "conventional composition" described in the '196 patent to treat rheumatoid arthritis.

The "conventional composition" is not Product R. The Examiner acknowledges that the "conventional composition" is made from a process different from the process producing Product R, but plainly ignores the fact that the two different processes result in two products having different properties by concluding that Product R and the "conventional composition" are the same product. The Examiner's conclusion is baseless, in view of the evidence based on the analysis of the physical, chemical and biological properties[2] of Product R and the "conventional composition".

No person of ordinary skill in the art, who is given the above evidence, would equal Product R to the "conventional composition".

Since the "conventional composition" is not Product R for the above reason, the "low molecular weight portion" of the "conventional composition" cannot be Product R.

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[2] These are inherent properties of Product R. A feature is inherent if it naturally occurs under the conditions set forth in the reference, even though the reference does not expressly mention the feature. *Tyler Refrigeration v. Kysor Industrial Corp .*, 777 F.2d at 689 [227 USPQ at 847].

2. The '196 patent fails to teach the administration route of the drug

Claim 1 requires a parenteral administration of Product R to treat rheumatoid arthritis, while the '196 patent mentions nothing with respect to administration route for the treatment of rheumatoid arthritis.

3. The '196 patent further fails to teach "... in a range from about 2.5 microliters to about 40 microliters per kilogram of body weight per day in a pharmaceutically acceptable formulation."

Claim 1 further requires Product R to be administered in a specified dosage regimen, i.e. "in a range from about 2.5 microliters to about 40 microliters per kilogram of body weight per day." Nowhere in the '196 patent is such dosage regimen mentioned.

Thus, claim 1 cannot be anticipated by the '196 patent because it does not teach each and every element recited in claim, i.e. the administration route, the dosage regimen and most importantly, Product R, for treating rheumatoid arthritis.

Claims 2-4 are not anticipated by the '196 patent under 35 U.S.C. 102 (e) for the same reason as for claim 1.

III. The Claim Language "an effective symptom ameliorating amount of Product R in a range from about 2.5 microliters to about 40 microliters per kilogram of body weight per day" Is Clear and Definite.

The Examiner objects the claim language in claim 1 "an effective symptom ameliorating amount of Product R in a range from about 2.5 microliters to about 40 microliters per kilogram of body weight per day" solely because Product R is not quantified in terms of concentrations despite applicant's repeated explanation, both in the specification and in the responses to the Office Actions, that Product R exists in the liquid form and is preferably used in its original liquid form. In other words, Product R is the entire solution produced from the manufacturing

process, not any individual substance in the solution. It is undiluted nor contains any other additives. Thus, the concentration of the Product R is 100%.

A liquid substance is usually measured by volumes. For example, liquid HCl or liquid acetic acid can be measured as 2 ml of 3 ml, etc. In such instances, indication of the liquid concentration is unnecessary unless the liquid substance is diluted.

Product R is an undiluted liquid substance that is clearly described and defined in the present application. See Spec. pp. 10-13. A patentee is free to be his or her own lexicographer. "When the specification states the meaning that a term in the claim is intended to have, the claim is examined using that meaning..." *See MPEP* 2173.05(a).

There is nothing unclear about the claim language "an effective symptom ameliorating amount of Product R in a range from about 2.5 microliters to about 40 microliters per kilogram of body weight per day", had the Examiner recognized and accepted the fact that Product R is a substance in a liquid form made according to a specific process described in the application. Unfortunately, the Examiner erroneously treated Product R as a solid substance dissolved in a solution in making her determination.

Thus, claim 1 is definite under 35 U.S.C. 112, second paragraph.

Claims 2-4 are definite under 35 U.S.C. 112, second paragraph, for the same reason as for claim 1.

IV. Conclusion

The rejections to claims 1-4 under 35 U.S.C. 102 (e) as being anticipated by U.S. Pat. No. 5,849,196 to Kochel and under 35 U.S.C. 112, second paragraph, as being indefinite for failure to particularly point out and distinctly claim the subject matter which applicant regards as the invention should be withdrawn.

For the foregoing reasons, it is respectfully submitted that appellant's appellants' claims are not rendered obvious anticipated by and are, therefore, patentable over the art of record, and the Examiner's rejections should be reversed.

Respectfully submitted,
COHEN, PONTANI, LIEBERMAN & PAVANE

By _____
Yunling Ren
Reg. No. 47,019
551 Fifth Avenue, Suite 1210
New York, New York 10176
Tel (212) 687-2770

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APPENDIX

Claims

1. A method of ameliorating a symptom of rheumatoid arthritis in a patient suffering from rheumatoid arthritis, comprising parenterally administering to said patient an effective symptom ameliorating amount of Product R in a range from about 2.5 microliters to about 40 microliters per kilogram of body weight per day in a pharmaceutically acceptable formulation.

2. The method of claim 1 wherein said Product R is administered in a range from about 5 microliters to about 25 microliters per kilogram of body weight per day.

3. The method of claim 1 wherein said Product R is administered in amount of about 7.5 microliters per kilogram of body weight per day.

4. A method of ameliorating a symptom of rheumatoid arthritis in a patient suffering from rheumatoid arthritis, comprising the steps of:

a. parenterally administering Product R to said patient an effective symptom ameliorating amount of about 1 ml twice per day in a pharmaceutically acceptable formulation for about 15 days; and

b. parenterally administering Product R to said patient an effective symptom ameliorating amount about 1 ml once per day in a pharmaceutically acceptable formulation for about 75 fays after step a.